

Can Hematological Findings of COVID-19 in Pediatric Patients Guide Physicians about Clinical Severity?

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To the Editor,

The COVID-19 pandemic originated in December 2019 in the city of Wuhan, the capital of the Hubei province of China. Since then, the epidemic spread to numerous other countries in Asia and by January 2020 infected patients were identified in Europe (1). Children of all ages are susceptible to SARS-CoV-2 infection. Most children have relatively mild clinical symptoms without fever or pneumonia (2-8).

We conducted a retrospective study at Health Science University Izmir Behcet Uz Children Hospital, between 30 March and 31 October, 2020.

Totally 3878 pediatric patients were tested and 353 (9.1%) of them was diagnosed as COVID-19. Of the 353 children, 184 (52.1%) was male (52.1%), (female/male: 0.91). Median age of the patients was 9 years (4 day-17 years). Thirty five (9.9%) patients had underlying disease, most commonly neurological disease (n=9). Regarding the severity; 9 (2.5%), 293 (83%), 38 (10.8%), 13 (3.7%) cases were diagnosed as asymptomatic, mild, moderate, severe/critical respectively. Neutropenia (47.9 %) was the most common abnormal parameter in the complete blood count, followed by lymphocytosis (22.4 %), lymphopenia (20.7 %), leukopenia (9.1 %), neutrophilia (6.5 %) and thrombocytopenia (3.4 %) (Table 1).

Neutropenia was statistically significantly more common in neonates (84.6 %).

Lymphocytosis and neutrophilia were statistically significantly more common in infants [75.9%, p<0.001 and 23.3% p<0.001, respectively]. Lymphopenia and leukopenia were statistically significantly more common in patients >11 years old [38.4%, p<0.001 and 15.2%, p= 0.025, respectively]. Patients >11 years of age-old were more commonly thrombocytopenic, but not statistically significant (p=0.17).

Neutrophil-to-lymphocyte ratio (NLR) was higher in severe/critical patients compared to asymptomatic, mild and moderate disease severity patients [NLR in asymptomatic, mild,

moderate, and severe patients were as follows; 0.84 (0.2-3), 1.12 (0.04-28), 1.32 (0.11-4.6), 3.39 (0.23-10) respectively, p=0.25]

The platelet to lymphocyte ratio (PLR) statistically significantly increased as age increased. Lymphocyte to white blood cell ratio statistically significantly decreased as age increased. Lymphocyte to white blood cell ratio was lower in severe/critical patients compared to asymptomatic, mild and moderate disease severity patients. Red cell distribution width (RDW) statistically significantly increased in severe patients [asymptomatic, mild, moderate, and severe patients were as follows; 12.3 (12-13.1), 12.9 (11.2-13.2), 12.9 (11.6-19.5), 14.9 (13-19.6), respectively, p=0.005]. Median serum ferritin and d-dimer were statistically significantly increased in severe patients. Increased serum d-dimer was found to increase risk of disease severity 2.9 fold (%95 CI:0.13-0.85, p=0.022).

In our study results NLR ratio was higher in severe/critical patients compared to asymptomatic, mild and moderate disease severity. Qin et al have reported an increase in NLR in patients with severe disease compared to those without (8). In our results, RDW levels were significantly higher in severe patients. In an adult study authors conclude that, elevated RDW at the time of hospital admission and an increase in RDW during hospitalization were associated with increased mortality risk for patients with COVID-19, compatible with our results (6,9,10).

We recommend clinicians closely monitor leucocyte count, lymphocyte count, platelet count, serum d-dimer, serum ferritin, RDW as markers for potential progression to critical illness.

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Table 1. Comparisons of hematologic and biochemical parameters of patients according to disease severity					
	Asymptomatic	Mild	Moderate	Severe/Critical	P value
Hemoglobin (gr/dL)*	13.5 (8.9-14.3)	12.5(8.9-11.5)	12.3 (6.6-16)	8.9(2.5-13.1)	0.001
Leucocyte (x10³/μL)*	6.4 (2.8-12.5)	6.0 (3.0-25.2)	6.0 (2.2-19.2)	9.9(4.0-13.1)	0.39
Leukocytosis*	1(11.1)	14(5.6)	6(15)	2(28.6)	0.011
Leucopenia**	2(22.2)	24(9.5)	6(15)	0(0)	0.79
ANC (x10³/μL)*	2.4(0.86-3.7)	2.6 (0.11-17.7)	2.7 (0.16-10.9)	6.8 (0.7-10.3)	0.12
Neutropenia**	7(77.8)	138(54.8)	22(55)	2(28.6)	0.174
ALS (x10³/μL)*	2.2(1.2-9.1)	2.2(0.23-14.6)	2.7(0.7-8.2)	1.7(0.68-6)	0.93
Lymphocytosis**	4 (44.4)	61(24.3)	12(30)	2(28.6)	0.90
Lymphopenia**	2(22.2)	56(22.3)	12(30)	3(42.9)	0.13
Platelets *(x10³/μL)	321(128-547)	263(52-595)	258(146-665)	196(55-358)	0.15
Thrombocytopenia**	1(11.1)	6(2.4)	2(5)	3(42.9)	0.001
Neutrophil to lymphocyte ratio*	0.84 (0.2-3)	1.12 (0.04-28)	1.32 (0.11-4.6)	3.39 (0.23-10)	0.25
Platelet to lymphocyte ratio*	114 (59-301)	110 (24-830)	126 (38-268)	101 (0-287)	0.82
Lymphocyte to white blood cell ratio*	0.48 (0.22-0.73)	0.39 (0.03-0.92)	0.37 (0.16-0.70)	0.22 (0.09-0.61)	0.27
RDW (%)*	12.3 (12-13.1)	12.9 (11.2-13.2)	12.9 (11.6-19.5)	14.9 (13-19.6)	0.005
MPV (fL)*	9.5 (8.5-11.5)	9.8 (8-13.6)	9.7 (8.2-11.7)	10.7 (8.7-12.8)	0.15
PDW (%)*	9.3 (8.5-14.9)	10.6 (7.3-22)	10.5 (8.1-14.8)	13.6 (7.6-16.8)	0.26
Protrombin time (second)*	13.2 (9.5-14.1)	12.8 (9.4-17.7)	13(11-16.4)	14.7(12.9-20.9)	0.037
Increased PT**	0(0)	10 (6.7)	1(3.4)	4(33.3)	
aPTT (seconds)	29.6 (24.3-35.8)	31.9 (17.9-61.10)	31.2 (21.5-39.1)	31.3 (23.7-46)	0.91
Fibrinogen (mg/dL)*	224 (189-409)	260 (136-967)	273 (100-510)	374 (98-510)	0.26
Serum d-dimer (ng/mL)*	180(150-231)	150(70-3145)	150(150-1887)	1235(394-3037)	<0.001
Increased d-dimer**	0(0)	25(17.1)	7(22.6)	6(100)	<0.001
Serum ferritin (μg/L)*	16.9 (9.5-48.8)	40.2 (3-343)	39.8 (16.6-137)	134 (44-2051)	0.003
Increased ferritin**	0(0)	9(11.8)	2(10)	3(42.9)	

ANC: Absolute Neutrophil count, ALC: Absolute lymphocyte count, RDW: Red cell distribution width, MPV: Mean platelet volume, PDW: Platelet distribution width, aPTT: Activated partial thromboplastin time
 *:Median(min-max), **: n(%)

Uncorrected proof